REMARKS

Status of the Claims

Claims 1, 3-5, 11-14 and 18-26 are pending in the application. Claims 1, 3-5, 11-14 and 18-26 are currently amended; claims 2, 6-10 and 15-17 are canceled; and claims 18-26 have been added.

Claims 1-5 and 12-14 have been amended for grammar.

Claims 2 and 15-17 are canceled.

Claim 1 has been amended to specify that the instantly claimed pharmaceutical composition consists essentially of G-CSF and PlGF. Support for this amendment is found on page 4, lines 21-26 of the Specification.

Claim 11 has been amended to recite a method for stimulating blood cell mobilization in a patient in need thereof because said patient has undergone at least one procedure selected from a group of therapies or conditions comprising administering a pharmaceutical composition consisting essentially of granulocyte colony stimulating factor (G-CSF) and placental growth factor (PlGF) to said patient. Support for this amendment is found in the Specification on page 5, lines 9-17 and in the originally filed claims.

New claim 18 has been added, and recites that the combined preparation of claim 1 provides a synergistic activation of proliferation of the circulating white blood cells. Support for this claim is found in Example 1.

New claim 19 has been added, and it recites that the combined preparation of claim 1 provides a synergistic activation of proliferation of colony forming cells. Support for this claim is found in Example 3.

New claim 20 has been added, and it recites that the combined preparation of claim 1 provides a synergistic activation of proliferation of circulating long-term colony initiating cells. Support for this claim is found in Example 4.

New claim 21 has been added, and it is directed to a combined pharmaceutical preparation comprising G-CSF and PlGF that provides synergistic activation of proliferation of circulating white blood cells, circulating colony forming cells and of circulating long-term colony initiating cells. Support for this claim is found in Examples 1, 3 and 4.

New claim 22 has been added, and it is directed to a method for increasing the numbers of circulating white blood cells, colony forming cells or long-term colony initiating cells comprising administering to a subject an effective amount of a pharmaceutical composition comprising G-CSF and PlGF. Support for this claim is found in Examples 1, 3 and 4.

New claim 23 depends from claim 22, and further recites that the proliferation of a circulating white blood cells, colony forming cells and long-term colony initiating cells is increased in a synergistic manner. Support for this claim is found in Examples 1, 3 and 4.

New claim 24 has been added. It is directed to a method for stimulating blood cell mobilization in a patient comprising administering, either simultaneously or separately, a pharmaceutical composition consisting essentially of G-CSF and placental growth factor PlGF to said patient. Support for this claim is found on page 5, lines 17-23 of the Specification and in the original claims.

New claim 25 depends from claim 11, and recites that G-CSF and PlGF are administered simultaneously, separately at intervals or sequentially. Support for this claim is found in the Specification at page 17, line 16 to page 18, line 9.

New claim 26 is directed to a kit for the combined administration of G-CSF and PlGF; simultaneous or separate administration of the active ingredients of the "combined preparation" is described at, e.g. page 5, lines 18-20. Plainly the latter requires separate packaging of the two active ingredients.

No new matter has been added.

1. Claim Rejections under 35 U.S.C. § 112, 2nd Paragraph

The Examiner has rejected claims 2 and 11-16 as allegedly indefinite. The Examiner's detailed reasoning for these rejections appears on page 2 of the Office Action, and is not reproduced here. Applicants have canceled claim 2 and amended claim 11, thereby obviating the rejection.

2. Claim Rejections under 35 U.S.C. § 112, 1st Paragraph-Enablement

The Examiner has rejected claims 11-14 as allegedly not enabled. The Examiner admits that the Specification is enabling for a method of using the presently claimed composition as part of a treatment (*e.g.* mobilization of cells during the recovery phase of a disease, etc.), but contends that the Specification is not enabling for the complete treatment of disease. (Office Action, page 3). Although Applicants do not agree with the Examiner, at least because it is not clear to Applicants how use as a part of a treatment is nonetheless not a treatment, Applicants have amended claim 11, thereby obviating the rejection.

3. Claim Rejections under 35 U.S.C. § 103

3(a) Bahlmann et al. and Robinson et al.

The Examiner has rejected claims 1-3, 11, 13 and 17 as allegedly obvious over Bahlmann et al. (US 2005/0272634) in view of Robinson et al. (Office Action pages 5-8). Applicants respectfully traverse.

Bahlmann teaches compositions comprising erythropoietin (EPO) and at least one other ingredient selected from the group consisting of VEGF, PlGF, GM-CSF or HMG-CoA reductase inhibitors for promoting the production of red blood cells and endothelial cells. It follows that any composition taught by the combination of Bahlmann and Robinson that contains PlGF and G-CSF must also include EPO. The Examiner cites Robinson as allegedly teaching that GM-CSF and G-CSF are functional equivalents*.

* Applicants do not agree with the Examiner's assertion; but, even if it is the case that GM-CSF and G-CSF are functional equivalents, then the combination of Bahlmann and Robinson teaches away from the presently claimed invention. If the Examiner's assertion were true, the Bahlmann – Robinson combination would teach that a

Applicants have amended claim 1 to recite a pharmaceutical preparation "consisting essentially of" G-CSF and PlGF. Accordingly, claim 1 is directed to compositions that contain these two substances and only such other ingredients as do not affect the essential utility of the presently claimed composition: *i.e.* the mobilization of peripheral blood progenitor cells (PBPCs). Applicants submit that the EPO included in the above-discussed Bahlmann – Robinson taught composition is a utility altering ingredient, in that at least stimulation of red blood cell production would occur in addition to mobilization of PBMCs.

In other words, the Bahlmann – Robinson taught composition of EPO, G-CSF and PlGF contains different ingredients and is useful for a different purpose as compared to the presently claimed G-CSF / PlGF compositions. The combination of Bahlmann and Robinson therefore does not teach the presently claimed composition.

In summary, Applicants submit that the combination of Bahlmann and Robinson fails to teach the instantly claimed pharmaceutical composition, and also teaches away from the methods for stimulating PBPC mobilization of the present invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

3(b) Bahlmann et al., Robinson et al., Carmeliet et al., Freireich et al. and Kadar et al.

The Examiner has rejected claims 1-4, 11, 13 and 15-17 as allegedly obvious over Bahlmann et al. and Robinson et al., as applied to claims 1-3, 11, 13 and 17, in further view of Carmeliet et al. and Freiereich et al. The Examiner has also rejected claims 1-5 and 11-17 as allegedly obvious over Bahlmann, Robinson, Carmeliet and Freiereich in further view of Kadar et al. The Examiner's detailed reasoning for this rejection appears on pages 8-10 of the Office Action, and is not reproduced here. Applicants respectfully traverse.

As discussed above, the combination of Bahlmann and Robinson fails to teach the presently claimed invention, and the Carmeliet, Freireich and Kadar references provide no teachings that rescue those deficiencies. In particular,

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pharmaceutical composition containing EPO, G-CSF and PlGF stimulates red blood cell and endothelial cell production, not the presently claimed mobilization of PBPC.

- Carmeliet teaches the use of PlGF to treat ischemia and strokes, and is silent with respect to G-CSF.

- Freireich teaches correlating the maximum tolerable dose of toxic substances in animal models to that in man, and is silent with respect to both G-CSF and PlGF.

- Kadar teaches the use of G-CSF for mobilizing peripheral mononuclear blood cells in allogenic transplantation programs, and is silent with respect to PlGF.

Accordingly, no prior art reference teaches the presently claimed compositions that consist essentially of PlGF and G-CSF. No prior art reference teaches the presently claimed method for stimulating blood cell mobilization by treating a patient with PlGF and G-CSF without additional active ingredients. It follows that even the combined teachings of Bahlmann, Robinson, Carmeliet, Freireich and Kadar fail to teach the presently claimed invention, and the Examiner has not established a *prima facie* case of obviousness. Applicants therefore respectfully request reconsideration and withdrawal of these obviousness rejections.

4. Double Patenting

The Examiner has indicated that, should claim 3 be found allowable, claim 17 will be objected to under 37 CFR § 1.75 as a substantial duplicate of claim 3. (Office Action page 10). Applicants have canceled claim 17, thereby obviating the rejection.

5. Conclusion

In view of the forgoing amendments and remarks, Applicants respectfully request allowance of all the claims, which are drawn to subject matter that meets all statutory patentability requirements.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By /mjn/
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